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**Quality of life in patients receiving telemedicine enhanced chronic heart failure disease  
management: A meta-analysis**

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**Abstract**

**Background:** Previous reviews have investigated the effectiveness of telemedicine in the treatment of heart failure (HF). Dependent variables have included hospitalizations, mortality rates, disease knowledge and health costs. Few reviews, however, have examined the variable of health-related quality of life (QoL).

**Methods:** Randomized controlled trials comparing the delivery methods of any form of telemedicine with usual care for the provision of HF disease-management were identified via searches of all relevant databases and reference lists. To be included studies had to report a quantitative measure for mental, physical or overall QoL.

**Results:** 33 studies were identified. However, poor reporting of data resulted in the exclusion of 7, leaving 26 studies with 7,066 participants. 3 separate, random effects meta-analyses were conducted for mental, physical and overall QoL. Telemedicine was not significantly more effective than usual care on mental and physical QoL (SMD 0.03, (95% CI -0.05-0.12),  $P = 0.45$  and SMD 0.24, (95% CI -0.08-0.56),  $P = 0.14$ , respectively). However, when compared to usual care, telemedicine was associated with a small significant increase in overall QoL (SMD 0.23, [95% CI 0.09-0.37],  $P = 0.001$ ). Moderator analyses indicated that telemedicine delivered over a long-duration ( $\geq 52$  weeks) and via telemonitoring was most beneficial.

**Conclusion:** Compared to usual care, telemedicine significantly increases overall QoL in patients receiving HF disease management. Statistically non-significant but nonetheless positive trends were observed for physical QoL, also. This provides preliminary support for the use of telemedicine in the management of heart failure without jeopardising patient well-being.

### **Keywords**

Telemedicine, heart failure, disease management, quality of life, meta-analysis

### **Introduction**

It was recently estimated that over 23 million people worldwide were living with heart failure (HF)[1]. The chances of developing the condition are estimated one in five [1], there is a high prevalence of re-hospitalization [2], and a high five-year mortality rate [3, 4]. Disease management programs have therefore been designed to stem the ever-rising costs associated with HF.

Whilst disease management programmes have been shown to decrease mortality and hospital readmissions associated with HF [5-7], uptake to these programmes is extremely low. In the UK, the National Audit of Cardiac Rehabilitation [8] reported that fewer than 4% of all patients presented with HF as a primary diagnosis, despite 88% of cardiac rehabilitation centres offering support for this

disease. Studies investigating low uptake to treatment have identified patient-related factors such as a lack of time or transport as common barriers [9, 10].

Telemedicine has the potential to alleviate problems of access to treatment for HF, especially in rural communities. Telemedicine is defined by the World Health Organisation [11], as 'The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries...' (P9). By allowing a medical practitioner to communicate with a patient remotely, the problems of transport and time are largely overcome. Research has shown telemedicine can significantly reduce both mortality and re-hospitalization rates [12, 13]. Additionally, home-based telemedicine can not only support health behaviour change, but can enhance disease-specific education and increase patient's self-care. All of these may substantially reduce the burden on practitioners [14], and potentially reduce healthcare costs [15, 16].

Published reviews of telemedicine have investigated multiple health-related variables, such as, hospitalizations, mortality rates and disease knowledge. To our knowledge, no recent published meta-analytic review has synthesised research investigating the effectiveness of telemedicine versus usual care on health-related quality of life (QoL) in the treatment of HF. This is despite relationships between low QoL and poor HF outcomes [17, 18]. Although Inglis et al., [12] have published some exemplary reviews which they have continued to update, the authors only describe and tabulate QoL and so do not include the variable in their meta-analysis. The aim of this systematic review is to synthesise research reporting the effects of telemedicine on the self-reported QoL of patients with HF.

## **Method**

### **Inclusion criteria**

Whilst the risk of publication bias is always an issue [19], we believe that the results from large multi-centred published studies using rigorous methods could be diminished by the inclusion of unpublished studies. Furthermore, inclusion of the latter might increase the heterogeneity of the findings, rendering the aggregation of these via meta-analytical methods less reliable. We therefore only included published data. In further efforts to maintain the reliability and rigor of our analysis, we only included studies reporting the findings of randomised controlled trials (RCTs).

### *Search strategy*

Keywords were “telemedicine”, “telehealth”, “telemonitoring”, “cardiac”, “cardiovascular”, “heart”, “rehabilitation”, “disease-management”, “intervention” and “secondary prevention”. These were entered into databases using the Boolean operators “AND” and “OR” to retrieve studies most appropriate to providing an overview of telemedicine in HF. Studies were selected if the articles contained the keywords anywhere in the text. Databases searched were: PubMed, Web of Science, Medline, Cochrane Library, Excerpta Medica Database (EMBASE), National Institute for Health Research (NIHR), Centre for Reviews and Dissemination (CRD), Database of Abstracts of Reviews of Effects (DARE), Psych Articles, Primo, Scopus and Google Scholar. Relevant journals, such as the Journal of Telemedicine and Telecare, the Journal of Cardiac Failure, and the European Journal of Cardiovascular Nursing were searched for studies not identified by the above searches. Reference lists of relevant studies and critical reviews were hand-searched. All searches were up to and including May, 2016.

### *Study selection*

It is not surprising, given the multiple methods of telemedicine available, that a cursory review of the relevant literature reveals substantial methodological heterogeneity. We therefore set the following inclusion criteria. Studies were included in the meta-analysis if they were RCTs comparing *any* form of telemedicine delivered directly to a HF population, with standard post-discharge usual care.

Studies had to be published in a peer-reviewed journal and report a quantitative measure of QoL.

Any questionnaire measuring QoL was acceptable. Studies had to be written in English. We excluded studies conducted on the caregiver as opposed to the patient, and those that used a primary-prevention population.

#### *Data collection*

The first author checked the title and abstract of each study identified against the inclusion/exclusion criteria. Full-text articles were retrieved and assessed. For studies included in the analysis, all relevant information was extracted, and SPSS v21 was used to store and categorise variables. Two authors applied the guidelines presented in SIGN-50 [20] to gauge the quality of the study; where there was disagreement, the third author mediated discussion to gain consensus.

#### *Analyses*

The primary outcome variable was health related quality of life (QoL), which was expressed via three components; mental, physical, and overall. Although a lack of clarity over the exact definition for the concept of QoL is evident [21, 22], Mental QoL refers to a patient's perceptions of social functioning, vitality and emotions, and Physical QoL refers to a patient's perceptions of pain, physical functioning and general health. Overall QoL involves aspects from both the mental and physical components [23-25].

If an individual study reports 2 different components of QoL, where appropriate the remaining component will be inferred.

Meta-analyses were conducted on each component of QoL separately. We used a random effects model and the standardized mean difference (SMD), and assessed heterogeneity using the Q statistic [26]. To mitigate for the Q statistic's lack of power with small samples and excessive power with large samples [27], the  $I^2$  index [28] was also used. On the basis of generally equivalent attrition rates observed between experimental and control conditions in all studies, and in the

absence of evidence for the otherwise, in studies reporting attrition between baseline and end-point, it was assumed that participants were missing completely at random (MCAR).

Standardized mean difference effect sizes were calculated using Hedges g [29] to accommodate different sample sizes across conditions. We employed the correction factor for positive bias proposed by Morris (equation 10) [30]. 95% confidence intervals were then calculated for each effect size (ES). Given between-study heterogeneity in relation to the reporting of statistical results, we needed to adopt several methods to calculate ES. Descriptions of each method are presented in Table 1. Forest and funnel plots were prepared using Review Manager 5.3.

### *Moderator analysis*

Moderator analyses were conducted to identify variables that significantly influenced overall ES. Two possible moderators were identified from previous research; firstly the method of delivery [13], and secondly the duration of the intervention [31]. For the former analysis, studies were grouped into telemonitoring (TM; the monitoring of vital signs from a distance using equipment such as digital scales or small PDAs), telephone (TP; regular scheduled phone calls to monitor or provide educational coaching to a patient) and miscellaneous (M; studies which do not solely fit into either of the 2 previous categories, such as regularly scheduled video-conferencing). For the latter, studies were grouped post-hoc into ' $\leq 13$  weeks', '>13 to <52 weeks' and ' $\geq 52$  weeks', in which analysis the groups are non-similar in duration to avoid underpowered analyses. A third moderator analysis that sought to investigate the effect of geographical location, specifically rural and urban groups, was planned to test the hypothesis that the effects of telemedicine might be more pronounced in a rural setting. However, in almost all of the articles, it was unclear how large the catchment area was for each study and thus none could be reliably classified geographically.

## **Results**

### *Study selection*

1,580 citations were identified and examined for relevance. Following exclusions, 266 studies remained and full-text copies were accessed. Details of the study exclusion process are presented in Figure 1.

A total of 33 studies met the inclusion criteria (Table 2). However, due to poor reporting of descriptive statistics required to calculate effect sizes, a further 7 studies were excluded [32-38]. This was despite attempts to contact the respective authors to secure missing data. A funnel plot is shown in figure 2 detailing the risk of bias in the meta-analyses, where a summary of this bias is included in table 2 using the SIGN-50 guidelines. 3 studies [57, 67, 71] compared two different forms of telemedicine to usual care and from this point forwards are thus referred to as two separate studies. The studies included 12 that reported overall QoL only, 5 that reported both mental and physical QoL, and 9 studies that reported all three components of QoL. Furthermore, 1 study reported overall and physical QoL and 1 study reported physical QoL only. 1 study that compared 2 forms of telemedicine [67] reported mental and physical QoL for one form of telemedicine (included in the total above) and only mental QoL for the other. A total of 5 included studies reported mental and physical but not overall QoL [47, 49, 54, 67, 72]. 4 of these studies used the SF-12/36 and thus an overall QoL score was not calculated, as the short form explicitly states that this is inappropriate. The remaining study used the MLHF questionnaire and did not report enough data for an overall score to be inferred. A total of 7,066 participants, from 10 different countries were included in the analysis. 16 of 29 studies, representing 3,515 participants, were conducted in the USA

A total of 10 different questionnaires were used to measure QoL in the included studies; the Minnesota Living with Heart Failure Questionnaire (MLHF) [39], both the 36 and 12 item Short Form (SF-36 and SF-12, respectively) [40], the 8-item Short Form Health Survey (SFHS-8) [41], the General Health Questionnaire (GHQ) [42], the Kansas City Cardiomyopathy Questionnaire (KCCQ) [43], the Hospital Anxiety and Depression Scale (HADS) [44], the EuroQol (EQ-5D) [45] and the Psychological



General Well-Being Index (PGWBI) [46]. A Polish variant of the SF-36 was also used in 2 studies [60, 61].

Figure 1: Study selection flowchart

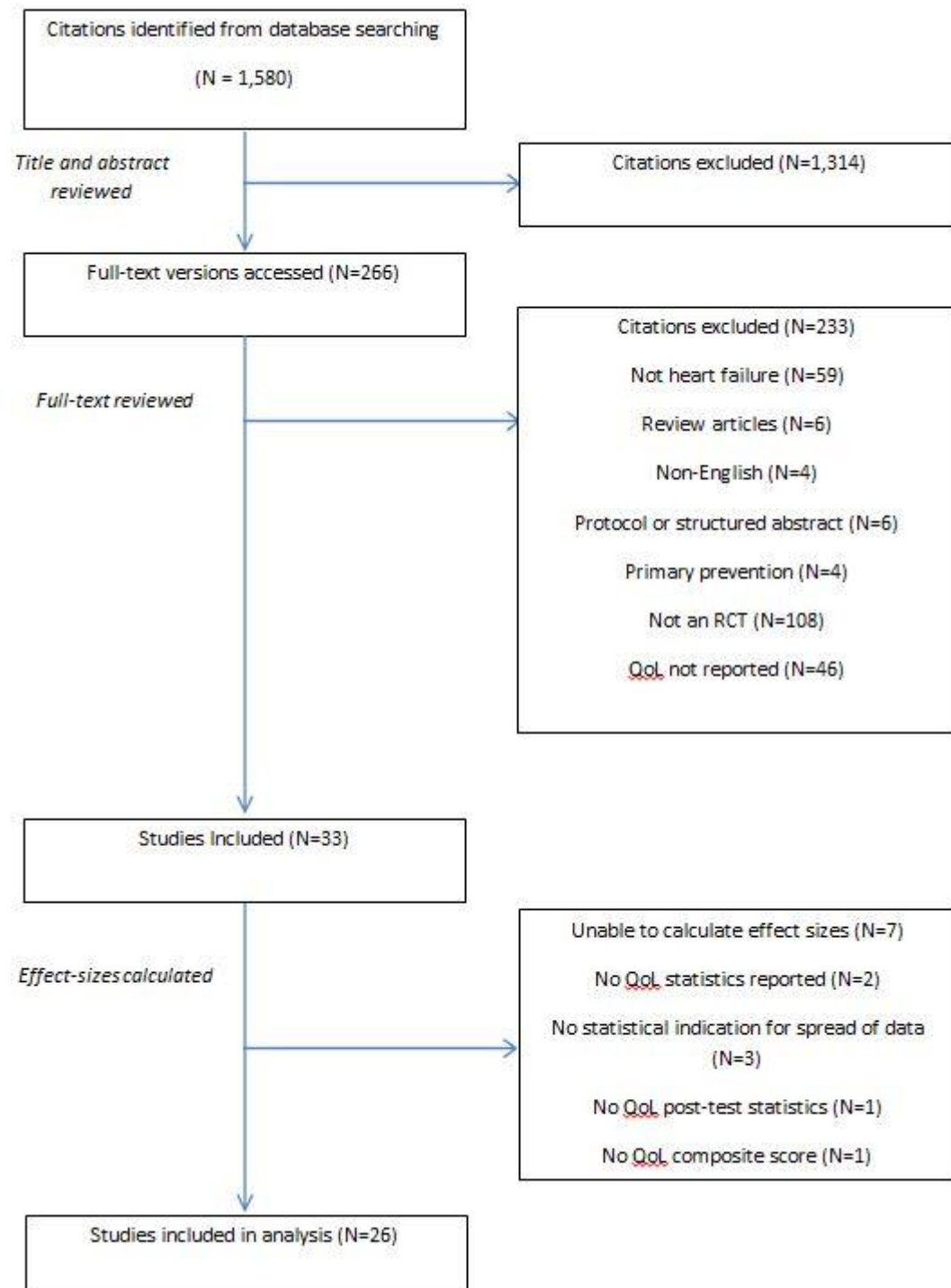


Table 2: Description of included studies

Study	Intervention	Duration of follow-up (weeks)	Number of patients	Mean age (years)	Male sex (%)	Country	Type of QoL (Questionnaire used)	Sign-50
Antonicelli, et al. (2008) [47]	Telemonitoring	52	57	78	61.5	Italy	Mental + Physical (SF-36)	+
Artinian, et al. (2003) [48]	Telemonitoring	13	18	68	94.5	USA	All (MLHF)	+
Barth, V. (2001) [49]	Structured telephone support	13	34	75	47	USA	All (MLHF)	+
Copeland, et al. (2010) [50]	Structured telephone support	52	458	70	99	USA	Mental + Physical (SFHS-8)	-
Dar, et al. (2009) [51]	Telemonitoring + telephone support	26	182	71	66.5	UK	Overall (MLHF)	++
De Lusignan, et al. (2001) [52]	Telemonitoring + video conferencing	52	20	75		UK	Overall (GHQ)	-
DeWalt, et al. (2006) [53]	Structured telephone support	52	123	63	49	USA	Overall (MLHF)	++
Dunagan, et al. (2005) [54]	Structured telephone support	52	151	70	43.5	USA	Mental + Physical (MLHF)	++
GESICA Investigators (2005) [55]	Structured telephone support	52	1518	65	71	Argentina	All (MLHF)	++
Goldberg, et al. (2003) [56]	Telemonitoring	26	280	59	67.5	USA	All (MLHF & SF-12)	+

Jerant et al. (2003) [57]	Structured video conferencing support	9	25	70	48	USA	All (MLHF)	++
	Structured telephone support		24	72	46			++
Koehler, et al. (2011) [58]	Telemonitoring	104	710	67	81.5	Germany	Physical (SF-36)	++
Madigan, et al. (2013) [59]	Telemonitoring	10	95	75	33.5	USA	Overall (KCCQ)	++
Piotrowicz et al. (2014) [60]	Telemonitoring	8	131	58	89.5	Poland	All (PSF-36)	+
Piotrowicz, et al. (2015) [61]	Telemonitoring	8	107	58	89	Poland	Overall (PSF-36)	+
Ramaekers, et al. (2009) [62]	Telemonitoring	13	101	72	61.5	Netherlands	Overall (HADS)	-
Riegel, et al. (2006) [63]	Structured telephone support	26	134	72	46.5	USA	All (MLHF)	++
Schwarz, et al. (2008) [64]	Telemonitoring	13	102	78	48	USA	Overall (MLHF)	++
Seto, et al. (2012) [65]	Telemonitoring	52	82	54	96.5	Canada	All (MLHF)	++
Sisk, et al. (2006) [66]	Structured telephone support	52	406	60	48.5	USA	Overall + Physical (MLHF & SF-12)	++
Smith, et al. (2005) [67]	Structured telephone support	78	715	71	72	USA	Mental (SF-36)	+
	Structured telephone support + telemonitoring		713	71	71		Mental + Physical (SF-36)	+
Stromberg, et al. (2006) [68]	CD-ROM based education	26	154	70	71	Sweden	Overall (EQ-5D)	+

Tomita, et al. (2009) [69]	Internet-based education	52	40	76	32.5	USA	Overall (CHFQ)	+
Villani, et al. (2014) [70]	Telemonitoring	52	80	72	74	Italy	Overall (PGWBI)	+
Wakefield, et al. (2008) [71]	Structured telephone support	26	96	70	99	USA	Overall (MLHF)	++
	Structured video conferencing support		101	68	98			+
Wootton, et al. (2009) [72]	Structured telephone support	52	409	83	68.5	Australia	Mental + Physical (SF-12)	+

SF-36: 36-Item Short Form; MLHF: Minnesota Living with Heart Failure Questionnaire; SFHS-8: 8-item Short Form Health Survey; GHQ: General Health Questionnaire; SF-12:

12-item Short Form; KCCQ: Kansas City Cardiomyopathy Questionnaire; PSF-36: Polish Version of the SF-36; HADS: Hospital Anxiety and Depression Scale; EQ-5D: EuroQoL;

CHFQ: Congestive Heart Failure Questionnaire; PGWBI: Psychological General Well-Being Index; ++: high quality; +: acceptable; -: low quality.

### *Overall QoL*

22 studies measured the effect of telemedicine on overall QoL (Figure 3). The MLHF was the most commonly used measure (N = 14). Telemedicine was found to be more effective than usual care in improving overall QoL in HF patients (SMD 0.23, [95% CI 0.09-0.37],  $P = 0.001$ ,  $I^2 = 34\%$ ). The Q statistic was non-significant at the  $P = 0.05$  level; this is supported by the  $I^2$  index showing only a low level of heterogeneity in the results (33.8%). Using Cohen's thresholds for interpreting effect sizes [73], 0.23 indicates a small positive effect for telemedicine when compared to usual care.

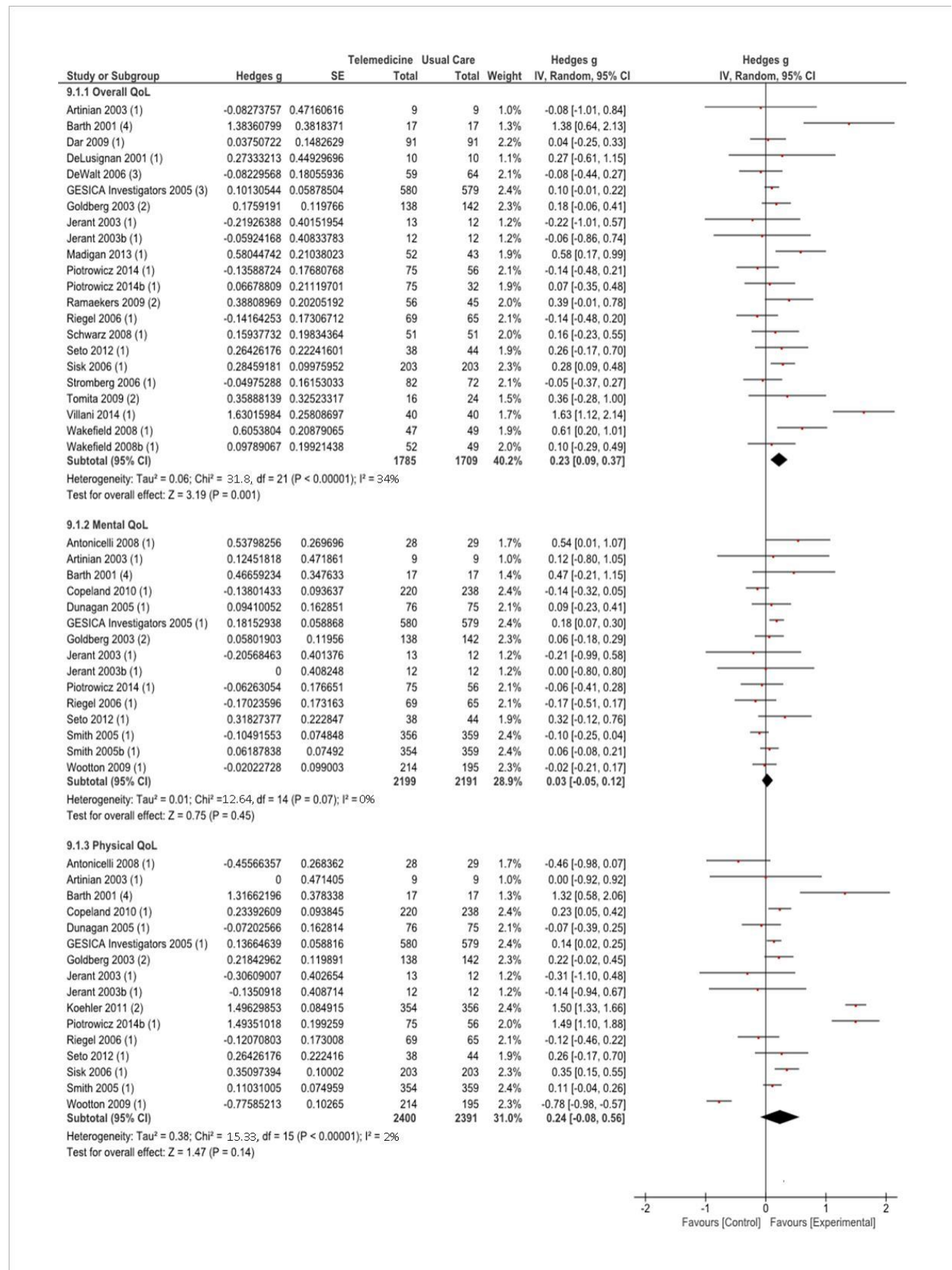
### *Mental QoL*

15 studies examined the effect of telemedicine on mental QoL. The two main measures used were the MLHF (N = 8) and 2 different itemed Short Forms (12, 36; N = 6). Random-effects meta-analysis indicated that telemedicine was equally effective as usual care in improving mental QoL (SMD 0.03, (95% CI -0.05-0.12),  $P = 0.45$ ,  $I^2 = 0\%$ ). The Q statistic was again non-significant at the  $P = 0.05$  level, with the  $I^2$  index showing no heterogeneity in the results also (0%).

### *Physical QoL*

16 studies examined the effect of telemedicine for heart failure on physical QoL. Similar to mental QoL, the MLHF and the 12 and 36 item versions of the Short Form, were the most common questionnaires used to measure physical QoL; with 8 and 7 studies using each questionnaire respectively. The aggregation of the effect sizes using a random-effects model indicated that telemedicine had a slightly larger effect than a usual care control condition, although this effect was not statistically significant (SMD 0.24, (95% CI -0.08-0.56),  $P = 0.14$ ,  $I^2 = 2\%$ ). The Q statistic was not significant at the  $P = 0.05$  level, which was supported by the  $I^2$  index being classified as low (2.1%).

Figure 3: Forest plot showing effect sizes for telemedicine vs. usual care



### *Moderator analyses*

In evaluating the moderating effects of the mode of telemedicine delivery, 11, 11 and 7 studies fell into TM, TP and M categories respectively. Studies in the M category were characterised by heterogeneous delivery methods. This category included studies which either used delivery methods that did not fit into the 2 previously mentioned categories (for example, video-conferencing or internet-based interventions) or methods that employed elements from *both* the TM and TP categories.

In TM a positive and significant effect on overall QoL was observed when compared to usual care (SMD 0.34, df = 8, P = 0.02). Contrastingly, no statistically significant effects were observed for TP (SMD 0.22, df = 6, P = 0.06) or M (SMD 0.04, df = 5, P = 0.62).

Effects on mental QoL were non-significant for TM (SMD 0.13, df = 4, P = 0.18), TP (SMD 0.00, df = 7, P = 1.00) and M (SMD 0.06, df = 1, P = 0.44). The M group however, incorporated only 2 studies and thus may be considered underpowered. Likewise effects on physical QoL, were non-significant for TP (SMD 0.07, df = 7, P = 0.68), and M (SMD 0.00, df = 1, P = 0.95), whilst a large effect size approaching statistical significance was observed for TM (SMD = 0.59, df = 5, P = 0.08). The M analysis was again conducted with only 2 studies.

A second moderator analysis evaluated the effect of intervention duration. For ease, the groups,  $\leq 13$ ,  $>13$  to  $<52$  and  $\geq 52$  weeks will henceforth be referred to as short, medium and long, respectively. Groups contained 9, 6 and 14 studies, respectively.

For overall QoL no significant effect of the short (SMD 0.23, df = 8, P = 0.09) or medium (SMD 0.10, df = 5, P = 0.25) durations was evident when compared to usual care. In long, a significant effect (SMD 0.37, df = 6, P = 0.02) indicated that over longer periods, telemedicine was more effective than usual care. Care must be taken in interpreting this result; however, as the  $I^2$  index showed that the long intervention length had substantial heterogeneity (61.5%). No significant effects for duration

were observed when comparing telemedicine to usual care in mental QoL (Short: SMD 0.02, df = 4, P = 0.88; Medium: SMD -0.02, df = 1, P = 0.84; Long: SMD 0.05, df = 7, P = 0.39) or physical QoL (Short: SMD 0.51, df = 4, P = 0.23; Medium: SMD 0.07, df = 1, P = 0.67; Long: SMD 0.15, df = 8, P = 0.48).

## Discussion

Findings indicate that telemedicine is not inferior to usual care in the maintenance of mental and physical QoL in patients with HF and is significantly more effective than usual care in maintaining overall QoL. Moderator analyses indicate that whilst TP and M are as effective as usual care, TM is more effective in the maintenance of QoL.

Although it is not clear why TM should be associated with a larger positive effect than TP and M, it could be due to the continuous support that TM is able to provide. This allows for early identification of complications or disease progression, and supports adherence to disease management programmes [74]. Within physical QoL, TM was also associated with a moderate SMD (0.59), suggesting that this delivery method is substantially more effective than usual care. This effect, although approaching significance (P = 0.08), was not statistically significant at the 0.05 level. Whilst this result became significant with a much larger effect when utilizing a fixed effects model, this approach does not facilitate generalizability and also works on the assumption that there is one single true effect [75]. Given the possible differential effect of study-level moderators (age of the patient, acceptance to technology, etc.), and the substantial heterogeneity between studies ( $I^2=96\%$ ), the use of random effects is warranted.

Previous studies have reported that although telemedicine requires initial financial investment, over a long period such interventions prove to substantially reduce medical costs [75]. Our moderator analysis for intervention duration indicated that although shorter duration interventions were not inferior when compared to usual care and thus there are clear reasons that such interventions may be adopted; telemedicine delivered over a long period ( $\geq 52$  weeks) was associated with a larger



effect than usual care, perhaps supporting both financial and ethical arguments for the broader adoption of telemedicine in this context.

The calculation of ES is straight forward, requiring as few as 2 means and standard deviations. The latest edition of the American Psychological Association publication manual describes the inclusion of these descriptive data-points as “essential” [77]. However, over and above the majority of studies failing to report the ES, almost 20% of studies meeting the inclusion criteria failed even to report data allowing ES to be calculated. Furthermore, of those that did, a wide variety of descriptive methods were reported requiring the use of multiple equations to calculate the statistic in question. This poor reporting of even the most basic descriptive data suggests that strict guidelines need to be implemented and enforced by journals to facilitate the systematic synthesis of findings, something that should be a core objective of all involved in research.

The methodological shortcomings of some of the included articles in this meta-analysis are not restricted to the under reporting of descriptive statistics. One advantage of the implementation of telemedicine direct to the home, is that patients do not need to travel for extended periods of time to attend disease management programmes; with the increased time it takes patients who live in rural areas to travel, or who face restrictions on movement due to disability, age, demographic or time constraints, this advantage is arguably multiplied. On the basis that most studies failed to report location, specifically patient location and/or hospital catchment areas, it is impossible to measure the efficacy of disease management delivered via telemedicine to rural patients. Future research should aim to rectify this situation so that possible geographical effects can be identified and researched further.

TM and TP delivery methods were used in over 75% of the included studies, and it is therefore hard to disagree with Kotb, et al.’s conclusions that the lack of data pertaining to less common delivery methods (for example, video-conferencing or internet-based interventions) is limiting our current understanding of their potential efficacy [13]. Future research should strive to increase the literature

on less common delivery methods, so that medical practitioners have available data on the positives and negatives associated with each mode of delivery.

In summary, data suggest that when compared with usual care, telemedicine is equally effective in the maintenance of physical and mental QoL but is more effective in relation to overall QoL. Our moderator analysis suggests that disease management received over a long duration via TM is most beneficial for overall QoL. This could be due to the continuous nature of TM facilitating early awareness of disease progression, and the longitudinal nature of TM promoting adherence to disease management programmes. This benefit is magnified by the increasingly low costs of TM compared to usual care over time [75]. These data provides preliminary support for the use of telemedicine in the management of heart failure without jeopardising patient well-being.

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## Appendices

Table 1: Effect size equations

Study reports	How effect size was calculated
1. Pre/post means and SDs	<p>Used</p> $g = \frac{(M_{post,T} - M_{pre,T}) - (M_{post,C} - M_{pre,C})}{SD_{pooled}},$ <p>Where M = mean, T = the treatment condition, C = the control condition and <math>SD_{pooled}</math> is given by</p> $SD_{pooled} = \left( \frac{(n_T-1)SD_{pre,T}^2 + (n_C-1)SD_{pre,C}^2}{n_T + n_C - 2} \right).$ <p>As described by Carlson and Schmidt (equation 1) [78].</p>
2. Mean change (delta scores) and SD of the change	<p>Used between groups, single test, Hedges g, given by</p> $g = \frac{M_T - M_C}{SD_{pooled'}}$ <p>where <math>SD_{pooled'}</math> is calculated as above accept using the SD of the mean change.</p>

<p>3. End-point p-values with no baseline differences</p>	<p>p-values were transformed into z-scores and then <math>g</math> was calculated by</p> $g = z \sqrt{\frac{n_T + n_C}{n_T n_C}}.$ <p>As described by DeCoster (equation 5.11) [79].</p>
<p>4. Paired sample t-statistic for each condition</p>	<p>Decoster [79] gives <math>g</math> from a <math>t</math>-statistic as</p> $g_j = \frac{t_j}{\sqrt{n_j}}.$ <p>Because the <math>t</math>-statistic here represents a paired sample, <math>g</math> is calculated separately for each condition and then combined using Becker's method [76], shown by:</p> <p><math>g = (c_T g_T) - (c_C g_C)</math>, where <math>g_T</math> and <math>g_C</math> = Hedges <math>g</math> for the treatment and control conditions, respectively and <math>c_T</math> and <math>c_C</math> are correction factors approximated by</p> $c_j = 1 - \frac{3}{4(n_j - 1) - 1}.$ <p>As detailed by Morris [27].</p>

Figure 2: Funnel plot assessing risk of bias

